

Convenor: Conny Nielsen, Denmark (for the first meeting)
Secretary: Lars Brogaard, Denmark

July 1999

D R A F T R E P O R T

of the 1st meeting of ISO/TC 84/WG 3 ad hoc 5 in Toronto, Canada
on Thursday, June 3, 1999, 9.00 a.m. - 1.00 p.m.

Comments on this draft report shall be sent to the secretariat before
August 20, 1999.

**LIST OF EXPERTS PRESENT AT THE 1ST MEETING OF
ISO/TC 84/WG 3/ ad hoc 5 "Needle-free injectors"**

COUNTRY	NAME	NOMINATED BY
DENMARK	Jørn Rex Hans Fhær Larsen	DS DS
GERMANY	Peter Kinast	DIN
NETHERLANDS	Ger J. van Keulen	NNI
SWEDEN	Bohdan Paulu	SIS-HHS
SWITZERLAND	Christoph Rindlisbacher	SNV
USA	Harold Yeager Paul E. Jansen Peggy Holland Linda D'Antonio Michael Roy Alan Felton	ANSI ANSI Invited Invited Invited Invited
DENMARK	Conny Nielsen Lars Brogaard	Convenor Secretary

1. Opening of the meeting

The preliminary convenor, Conny Nielsen, welcomed the experts to the meeting and thanked Eli Lilly and Becton Dickinson and Company for hosting the meeting.

2. Roll call of experts

The experts present and listed in this report presented themselves.

3. Approval of the agenda, doc. ISO/TC 84/WG 3/ ad hoc 5 N1

The draft agenda, doc. N1, was approved.

4. Report by the secretariat on the possibility of starting ISO-work on needle-free injectors

Lars reported that the proposal for a preliminary new work item had not obtained sufficient support. 9 P-members out of 20 were in favour, see below.

MEMBER BODY	APPROVAL		MEMBER BODY	APPROVAL	
Australia (SAA)	P	x	Netherlands (NNI)	P	x
Belgium (IBN)	P		Russian Federation (GOST R)	P	
Brazil (ABNT)	P		Slovakia (UNMS)	P	
China (CSBTS)	P	x	South Africa (SABS)	P	
Denmark (DS)	P	x	Spain (AENOR)	P	
France (AFNOR)	S	x	Sweden (SIS)	P	x
Germany (DIN)	P		Switzerland (SNV)	P	
India (BIS)	P		United Kingdom (BSI)	P	x
Ireland (NSAI)	P	x	USA (ANSI)	P	x
Italy (UNI)	P				
Mexico (DGN)	P				

The experts from Germany and Switzerland were of the opinion that DIN and SNV also would be in favour. They will be contacted to obtain a positive position which shall be given to the secretariat of ISO/TC 84 (Gisèle Sancho, AFNOR).

Anticipating that at least 11 countries will be in favour, the work can start and the ad hoc group decided to continue the meeting.

5. Discussion of main elements (safety, requirements and test methods) to be included in a possible ISO-standard for needle-free injectors

Jørn presented a list of different types of needle-free injectors. It comprised the following list based on characteristics:

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- Drug Compartment
(Liquid / Powder)
 - Single dose (single use Comp.)
 - Multidose (single use Comp.)
 - Refillable (automatic/manually)
 - Driving mechanism
(Power Source)
 - Spring
 - Gas
 - Compressed air
 - Nozzle
 - Multi use (durable)
 - Disposable

It also presented a proposal for safety and quality aspects to be considered by an ISO-standard.

Safety aspects:

- Visibility of drug when the pen-injector is ready for injection
- Residual scale
- Scale showing preset dose
- Visual indication of the pen-injector being ready for use
- Visual indication of the preset dose having been delivered
- Not possible to preset a larger dose than left in the cartridge - or indication of remaining dose
- No interchangeability with other systems

Quality aspects:

- Dose accuracy
- Physical preconditioning
- Cyclical preconditioning
- Test methods
 - Free fall
 - Chemical impact
 - Mechanical impact
 - Temperature impact

Jørn concluded his presentation by proposing that the term used should be "Needle-free injectors" and not "Jet injectors". This proposal was agreed.

Alan mentioned that the great difference and challenge in relation to the standards of pen-injectors would be the specification of requirements and test methods for the pressure profile of needle-free injectors.

He was, furthermore, of the opinion that it would be difficult to make a standard in consequence of the great variation in the constructions of needle-free injectors.

Paul agreed that it would be difficult to have all the product types included. Regardless of difficulties, he was of the opinion that the minimum clinical outcome for different medicinal products should be assessed. He mentioned that no clinical data on the effect by insulin injected by needle-free injectors exist.

Alan informed that the approval of needle-free injectors is carried out on a Grand Father basis and individual approval would be impracticable according to him.

Michael mentioned that the FDA seemed to intend to make use of a more individual approval in future and that the approval on the Grand Father basis is unacceptable in the long run.

Paul considered this as an argument for preparing an ISO-standard. It would be proactive as the industry can take part in specifying the essential requirements and test methods. He referred to the fact that the proposals for pen-injectors already have been in use for several years as the basis of the approval from authorities, which has been advantageous to all parties.

Alan mentioned that three main types of needle-free injectors exist. They are classified according to the depth in which they deliver the medicinal product:

- in the skin, or
- under the skin, or
- into the muscles

Bohdan suggested to go through the types of products to be covered by the standard. He pointed out the importance of determining whether the group should work with both single dose and multiple dose devices and the technology which is used to deliver the doses.

Jørn added that the most important task will be to ensure that the correct dose is given, e.g. by using in-vitro testing.

Paul said that methods might already be developed by manufacturers.

Linda replied that a test book is developed by PATH (The Programme for Appropriate Technology in Health). None of the participants had yet seen the test book but Linda would check up on where to buy it.

Paul suggested that the standard should not be covering issues on interchangeability, since it would not be considered relevant in connection with needle-free injectors. The standard ought only to be based on performances.

Linda asked if this would mean that interchangeability is prohibited. Paul explained that interchangeability will be permitted but that the standard will not specify dimensions for interchangeability.

Jørn emphasized the importance of not to discuss other issues than the performance at this stage. Later on it might be useful to examine interchangeability, which might be relevant in connection with a revision.

Ger suggested to prepare the scope and split the task into three aspects:

- mechanical aspects
- performance aspects
- user safety aspects

The group agreed that the preparation of the scope is the most important issue for proceeding the work, and the following shall be included:

- all types (depth into skin/mucosal)
- intra and extra cellular injection (depending on what you inject)
- not patches/infusers
- without needles, not hidden needles
- no penetration of the skin except by the medicinal product
- entire range of products (clinical use, ambulatory use)

After these considerations, the following draft scope was approved:

Draft scope

The standard specifies performance requirements and test methods for all needle-free injectors which actively force the medicinal product to penetrate the skin or mucosal membranes without any part of the device penetrating the membrane.

The standard covers devices intended for human use in clinics and for personal use.

The standard does not cover devices that apply passive delivery methods such as sprays, inhalators and liquid drops and patches.

The experts will comment on the draft scope before the next meeting.

It was noted that the benefit for the industry of making a standard will be:

- easier approval of products
- better foundation for product liability
- influence on requirements/test methods

The secretary explained the process of preparing an ISO standard, which includes the following:

Stages:

- | | |
|----------|--|
| Stage 0: | Preliminary work item stage (PWI) - No time limit |
| Stage 1: | Proposal stage - New work item proposal (NP) - A proposal for new work is circulated for a 3 month vote |
| Stage 2: | Preparatory stage - Working drafts (WD) |
| Stage 3: | Committee stage - Committee draft(s) (CD) - 3 month vote by participating members of the technical committee |
| Stage 4: | Enquiry stage - Draft International Standard (DIS) - Vote by all members of ISO for 5 month comments allowed |
| Stage 5: | Approval stage - Final Draft International Standard (FDIS) - Vote by all members of ISO - 2 month - Only Yes/No. |
| Stage 6: | Publication stage - International Standard |

6. Decisions on structure and headings to be included in a possible ISO-standard for needle-free injectors

It was decided to postpone the discussion until more information on existing devices are collected.

7. Organisation of future work

It was decided that information on existing devices shall be sent to the secretary for distribution to the group. This also applies to website addresses. Linda mentioned that she already had collected most of this information. Alan will contact PATH and ask them of their interest and possibility for participating.

The secretary mentioned that the American experts not yet nominated to participate in ISO/TC 84/WG3 should be formerly nominated by ANSI. The secretary will submit information to those not nominated.

8. Nomination of a project leader for needle-free injectors

Paul was proposed as project leader for needle-free injectors. Additionally, he was proposed as convenor for the ad hoc group, ISO/TC 84/WG3/ad hoc 5 - Needle-free injectors. He was elected unanimously for both tasks.

9. Date and place of next meeting

It was decided to hold the next meeting in September or October 1999 in the USA.

10. Any other business

Conny thanked the host once again for hosting the meeting.